REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and following remarks.

At the time of captioned Office Action, claims 1 and 21-72 were pending in the application. Without acquiescing to the propriety of the Examiner's rejections, Applicants have amended claims 1 and 32 and added new claims 73-78, to set forth the subject matter of the elected invention more clearly. Applicants also have revised claims 35 and 46 to correct informalities. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, are presented, with an appropriate defined status identifier.

These amendments do not go beyond the original disclosure of the application.

Method claims 21-31 and 33, drawn to non-elected invention, remain withdrawn from further consideration. Applicants respectfully request the rejoinder of these method claims pursuant to the *Ochiai/Brouwer* guidelines.

Upon entry of these amendments, claims 1 and 21 – 80 will be pending.

Claim Objection

Applicants have amended claim 35 to correct the informality pointed out by the Examiner. Accordingly, this objection is moot and should be withdrawn.

Claim Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants have revised claim 46 by deleting the phrase "anyone of." In view of this amendment, this rejection should be withdrawn.

Claim Rejection Under 35 U.S.C. § 102

The Examiner rejects claims 1, 32, 34-39, 41-49, 53, 55-61, 65-67, and 69-72 over Beudeker *et al.* (EP 0743017 A2). Specifically, the Examiner alleges that Beudeker discloses "an identical composition comprising [a] phospholipase." According to the Examiner, Beudeker's invention is "mainly drawn to an animal feed particularly plant based feeds comprising such enzyme, carriers and stabilizers required for use of the enzyme in the feed."

To negate novelty, a publication must disclose each and every limitation of the claimed invention. Applicants submit that Beudeker does not anticipate the claimed invention, within the meaning of Section 102, because it fails to disclose an enzyme that cleaves a phosphatidylinositol-containing linkage, effecting the release, in a pathogen, of a membrane-anchored protein or carbohydrate, such that the pathogen's ability to infect a host cell is reduced.

Beudeker exemplifies the use of phospholipase 2A, which does not cleave such a linkage. Rather, according to the Nomenclature Committee of the International Union of Biochemistry and Molecular Biology (NC-IUBMB), phospholipase A2 (EC 3.1.1.4) is a carboxylic ester hydrolase that acts on phosphatidylethanolamine, choline plasmalogen, and phosphatides, removing fatty acid attached to the 2-position and requiring Ca^{2+} (see Appendix 1 hereto). In other words, the enzyme expressly taught by Beudeker cleaves a fatty acid linkage, contrary to what independent claims 1 and 32 prescribe.

In addition, Beudeker's stated purpose is to "improve the emulsifying properties of phospholipids (e.g., lecithin) on the gastrointestinal tract and thereby improving the efficiency of feed and/or promoting the growth of the animal" (Beudeker at page 4, lines 3-5). In particular, Beudeker states that, "upon treatment with e.g., phospholipase A2, the HLB (hydropilic/lipophilic balance) value of lecithin is raised from 7 to approximately 8 or 9, which may contribute to the beneficial effects of phospholipase A2 treatment on the emulsification properties of lecithin" (*id.*, lines 41-42).

These teachings of Beudeker in no way implicate an enzyme that cleaves a phosphatidylinositol-containing linkage, as presently recited. In fact, the key enzymes in fat emulsification are pancreatic lipase and phospholipase A2, both of which degrade phospholipids, generating free fatty acids and a mixture of mono- and di-acylglycerols. (See Beudeker's Example 1, at page 7, lines 47 & 48, for the definition of "a unit of porcine phospholipase A2" as "the amount of enzyme producing one micromole of free fatty acid per minute under standard conditions....") Accordingly, no reading of Beudeker would have suggested, let alone anticipated, a scenario in which "cleavage effects release of [a] surface protein or carbohydrate," per claims 1 and 31. For this reason, Applicants request reconsideration and withdrawal of this rejection.

The Examiner cites Fodge *et al.* (WO 97/41739) against claims 32, 56-65, and 69-72, contending anticipation by Fodge's disclosing a composition comprised of a hemicellulase, such as mannanase or endo-1,4-β-D-mannanase, produced by *B. lentus* ATCC 55045.

Yet, as the present specification notes (page 11, first full paragraph), Fodge teaches a feed composition that combines a mannanase with an antibiotic. For example, the diets used in the pen trial to assess energy level effects contain SACOX and bacitracin MD (see Fodge's Table 8 at page 38, lines 10-30). Independent claim 32 contains a negative proviso that excludes the use of any anti-infection agent, including an antibiotic, that is other than the recited enzyme. Fodge therefore cannot anticipate claim 32 and its dependent claims, and the rejection should be withdrawn.

Claim Rejection Under 35 U.S.C. § 103

The Examiner rejects claims 39-40, 50, 52, 54-55 and 67-68 over Beudeker, as discussed above, in view of Kuppe *et al.*, *J. Bacteriol.* **17**: 6077 (1989), and Barbis *et al.*, *Brazilian J. Med. Biol. Res.* **27**: 401 (1994). The Examiner acknowledges that Beudeker does not teach the use of phosphatidylinositol-specific phospholipase C (PI-PLC) in a feed composition. The Examiner also relies on Kuppe and Barbis for teaching, respectively, that (a) PI-PLC can be purified from *B. cereus* and (b) PI-PLC treatment can render cells *in vitro* resistant to virus infection.

Thus, the Examiner is heard to allege that it would have been obvious to use the phospholipase C of Kuppe in a feed, per Beudeker, because of an expectation of anti-viral efficacy by Barbis.

Kuppe teaches cloning of PI-PLC from *B. cereus* into *E. coli* and extraction of PI-PLC from an *E. coli* preparation via a single ammonium sulfate precipitation step. A composition according to Kuppe's preparation would be physiologically unacceptable and unsuitable for oral administration, because it would be loaded with products harmful to humans and animals.

Kuppe's failure to suggest any *in vivo* therapeutic potential for phospholipase C is not remedied by Barbis. The latter publication teaches that pretreatment of

otherwise susceptible feline T cells with PI-PLC severely compromises the ability of canine parvovirus to infect the cells *in vitro*. There is no suggestion whatsoever that oral administration of phospholipase C might have a salutary impact.

In light of the secondary references, there would have been no motivation to employ phospholipase C as the "phospholipase" of Beudeker's feed composition. Indeed, Beudeker's stated purpose, namely, improving the emulsifying properties of phospholipids on the GI tract, actually leads away from the use of phopholipase C, which does not fulfill that purpose. Accordingly, the Examiner has not established *prima facie* obviousness, which warrants reconsideration and withdrawal of the rejection in question.

CONCLUSION

In view of the foregoing amendments and remarks, favorable reconsideration and allowance of this application are requested. An early notice in this regard is earnestly solicited. In the event that any issues remain, the Examiner is invited to contact the undersigned with any proposal to expedite prosecution.

Respectfully submitted,

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Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

APPENDIX 1

IUBMB Enzyme Nomenclature

EC 3.1.1.4

Common name: phospholipase A_2

Reaction: phosphatidylcholine + H_2O = 1-acylglycerophosphocholine + a carboxylate

Other name(s): lecithinase A; phosphatidase; phosphatidolipase; phospholipase A

Systematic name: phosphatidylcholine 2-acylhydrolase

Comments: Also acts on phosphatidylethanolamine, choline plasmalogen and phosphatides, removing the fatty acid attached to the 2-position. Requires Ca^{2+}.

Links to other databases: BRENDA, EXPASY, KEGG, WIT, CAS registry number: 9001-84-7

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[EC 3.1.1.4 created 1961, modified 1976, modified 1983]